Journal of Cardiovascular Computed Tomography 13 (2019) 113–117

Contents lists available at ScienceDirect

Journal of Cardiovascular Computed Tomography

journal homepage: www.elsevier.com/locate/jcct

Research paper

Diagnostic performance of free-breathing coronary computed tomography angiography without heart rate control using 16-cm z-coverage CT with motion-correction algorithm

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ARTICLE INFO

Keywords:
Coronary vessel
Tomography
X-ray computed
Free breathing
Breath holding

ABSTRACT

Objectives: To evaluate the feasibility of coronary computed tomography angiography (CCTA) in patients with free-breathing using 16-cm z-coverage CT with motion correction algorithm.

Methods: 616 patients underwent CCTA without heart rate control. 325 examinations were performed during breath-holding (group A), and the remaining 291 were performed during free-breathing (group B). The image quality scores were defined as 1 (excellent), 2 (good), 3 (adequate), and 4 (poor). 22 patients in group A and 24 in group B underwent invasive coronary angiography (ICA) after CCTA within two weeks. The image quality score, diagnostic accuracy using ICA as reference, signal-to-noise ratio (SNR), and effective dose (ED) were compared between the two groups.

Results: Mean heart rate during scanning was 70.8 ± 13.8 bpm in group A and 70.7 ± 13.2 bpm in group B (P = .950). No significant differences were observed in SNR and image quality score (1.49 ± 0.62 vs. 1.53 ± 0.67; P = .647) between the breath-holding and free-breathing groups. ED (1.99 ± 0.83 mSv vs. 2.01 ± 0.88 mSv) was not significantly different between the two groups (P = .975). In a segment-based analysis, the sensitivity, specificity and diagnostic accuracy in the detection of coronary stenosis of more than 50% were 82.1%, 96.8% and 92.2%, respectively in the breath-holding group and 82.2%, 96.6% and 92.2%, respectively in the free-breathing group with no significant differences for these parameters between the two groups.

Conclusions: CCTA for patients without heart rate control and during free-breathing using 16-cm z-coverage CT with motion correction algorithm showed no significant difference in image quality and diagnostic performance compared with CCTA during breath-holding.

1. Introduction

With continuous improvements in computed tomography technology, coronary computed tomography angiography (CCTA) has been established as a routine and noninvasive imaging method to rule out coronary artery disease as the cause of acute chest pain[1–5]. Traditionally, CCTA examinations are performed in a breath-holding state to reduce the artifacts caused by respiration. However, some patients cannot hold their breath (e.g. due to deafness, hearing weakness, severe pulmonary disease, agitation or lack of cooperativeness). For these patients, major stair-step artifacts often happen in the past that hamper the sufficient evaluation of the coronary arteries.[6] Therefore, it would be desirable to develop CCTA protocols during free breathing.

So far, the possibility of performing CCTA during free breathing has been reported on 320-detector CT with 16-cm z-axis coverage, and dual-source CT with high pitch scanning mode.[7,8] A main limitation of those studies is the restriction to patients with stable and low heart rates (e.g. < 75bpm or < 60 bpm). In our study, we investigated the feasibility of free-breathing CCTA without heart rate control using a 256-detector CT with 16-cm z-axis coverage and motion correction algorithm in terms of image quality, radiation dose and diagnostic performance.

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https://doi.org/10.1016/j.jcct.2019.01.005
Received 22 June 2018; Received in revised form 14 October 2018; Accepted 3 January 2019
Available online 04 January 2019

2. Methods

2.1. Study population

We prospectively enrolled 616 consecutive patients with chest pain referred for CCTA for ruling out coronary disease. Patients were randomly assigned to either free-breathing or breath-holding protocol: 325 CCTA examinations were performed using the traditional breath-holding method (group A), and 291 were performed during free-breathing (group B). Our local ethics committee approved this study; written informed consent for the CCTA procedure and for the research protocol was acquired from each patient after thorough explanation. 22 patients in group A (A_{ICA}) and 24 in group B (B_{ICA}) underwent invasive coronary angiography (ICA) after CCTA within two weeks. This study was approved by the ethics committee in our hospital, and written informed consent was acquired from each patient.

2.2. Imaging protocol

In this study, we used a 256-detector CT scanner (Revolution CT; GE Healthcare, Milwaukee, Wis) with z-coverage of 120, 140 or 160 mm dependent on patient heart size and secondary reconstruction with motion correction algorithm (snapshot freeze, SSF; GE Healthcare)to perform coronary CT angiography with the following characteristics: collimation, 0.625 mm; gantry rotation time, 280 ms. Tube voltage and current were determined by automatic exposure control system using baseline set at 120 kVp and noise index at 25 HU. Prospective ECG-triggered acquisition was performed within a single cardiac cycle. The acquisition windows were set at 70–80% of the R-R interval for patients with low heart rates (< 61 bpm), both 40–50% and 70–80% of the R-R interval for intermediate heart rates (61–75 bpm), and 40–60% of the R-R interval for high heart rates (> 75 bpm). The scanning range was from the level of the carina to the diaphragm.

All patients received a 50 mL bolus of contrast medium (370 mg of iodine per milliliter, iopromide; Ultravist, Bayer Schering Pharma, Berlin, Germany) via an antecubital vein at an infusion rate of 5 ml/s followed by 40 ml of saline solution. Imaging was performed by using the bolus tracking technique. Data acquisition was initiated with a 6s scan delay after the CT value reached a threshold of 100 Hounsfield units (HU) in a region-of-interest (ROI) in the descending aorta at the trachea bifurcation level. For group A, the breathing-holding command was given during the 6s delay and CCTAs were acquired with patients holding their breath after inspiration. For group B, the free-breathing CCTAs were performed with the same acquisition delay of 6s as group A but without interruption of breathing by muting the automatic play of breath-holding command. Before the free-breathing CCTA, patients were taught to breathe quietly throughout the whole examination.

2.3. Reconstruction and analysis of CCTA images

Images with both thickness and interval of 0.625 mm were reconstructed using hybrid iterative reconstruction algorithm (adaptive statistical iterative reconstruction-Veo, ASIR-V; GE Healthcare) with blending percentage of 50%. The cardiac phase with the least motion artifact was selected, and motion correction algorithm was applied in secondary reconstruction to further minimize motion artifact.

Reconstructed images were independently evaluated on an Advanced Workstation (ADW4.7, GE Healthcare, Waukesha WI USA) by two readers (Z.Z. and Y.S.) both with over 10 years of clinical experience in CCTA performance and analysis, blinded to the angiographic and clinical findings. Subjective image quality was evaluated using a 4-point Likert scale. Each segment was scored as excellent (no artifacts, score = 1), good (minor artifacts, good diagnostic quality, score = 2), adequate (moderate artifacts, acceptable for routine clinical diagnosis, score = 3) or poor (severe artifacts impairing accurate evaluation, segment classified as non-evaluable, score = 4). To determine the image quality, the coronary artery was subdivided into 15 segments according to the scheme proposed by the American Heart Association.[9] The whole coronary artery with a luminal diameter larger than 1.5 mm was analyzed.

CT attenuation values and their standard deviations in the descending aorta at the trachea bifurcation level were measured by using a ROI covering at least 75% of the vessel area avoiding calcification, plaques, and the stenotic wall. Based on these measurements, the signal-to-noise ratio (SNR) was calculated according to the following equations: SNR = CT attenuation value of aorta (HU)/standard deviation of aorta (HU).

An estimation of accuracy [sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV)] was calculated on a segment-based model based on a 50% threshold against the standard of ICA findings. The diagnostic performance between the two groups was compared using the pair wise McNemar's test. The inter-observer variability for the assessment of image quality and for the detection of significant disease on CCTA images were tested using the k test. A k value of less than 0.20 was considered to indicate slight agreement; a k value of 0.21–0.40, fair agreement; a k value of 0.41–0.60, moderate agreement; a k value of 0.61–0.80, substantial agreement; and a k value of 0.81 or greater, almost perfect agreement.

2.4. ICA procedure

Determined by the referral doctors according to clinical data, a total of 46 patients (22 patients in the breath-holding group and 24 in the free-breathing group)underwent both CCTA and ICA within two weeks. ICA was performed using a standard technique. The angiograms were analyzed by two interventional cardiologists (J.L. and C.C.) with more than 10 years of experience who were blinded to coronary CT angiography findings.

2.5. Radiation dose parameters

The effective dose (ED) of coronary CT angiography was calculated according to the European Working Group for Guidelines on Quality Criteria in CT.[10] The dose-length product (DLP) defined as the total radiation energy absorbed by the patient's body, was measured in mGy × cm in each patient. The effective dose (ED) was calculated as the dose-length product times a conversion coefficient for the chest (K = 0.014 mSv/mGy·cm).[11]

2.6. Statistical analysis

The breath-holding CCTA was defined as a reference standard protocol. Statistical analysis was performed by using SPSS software (version 22.0; SPSS, Chicago, Ill), and continuous variables were expressed as the mean ± standard deviation. Paired Student's *t*-test was used to test differences in continuous variables between the two groups, and the chi-squared test was used to study differences regarding categorical data. The diagnostic performance between the two groups was compared by using the pairwise McNemar's test. P-values lower than 0.05 were considered statistically significant. Inter-observer variability for the detection of significant stenosis (defined as any diameter stenosis > 50%) at coronary CT angiography and ICA were tested with Cohen k analysis. This analysis was performed on a per-segment level.

3. Results

The difference of the demographic data, including mean age, gender ratio, and body mass index, was not significant between the two groups. No significant differences were found between the two groups in terms of SNR, heart rate, and radiation dose. Table 1 shows the clinical characteristics of the study population and coronary CT angiography data.

Table 1
Comparison between the two groups for general characteristics, signal-to-noise ratio (SNR) and radiation doses.

	A	B	P-value
Sex (male/female)	179/146	168/123	0.507
Age (years)	64.1 ± 10.6	63.6 ± 9.5	0.793
BMI (kg/m^2)	25.23 ± 3.21	24.54 ± 3.17	0.815
Heart rates (bpm)	70.8 ± 13.8	70.7 ± 13.2	0.950
Minimum heart rate (bpm)	42	43	–
Maximum heart rate (bpm)	149	137	–
SNR	16.55 ± 4.65	15.61 ± 3.79	0.358
$CTDI_{vo\ 1}$ (mGy)	10.15 ± 4.32	10.17 ± 4.25	0.963
ED (mSv)	1.99 ± 0.83	2.01 ± 0.88	0.975

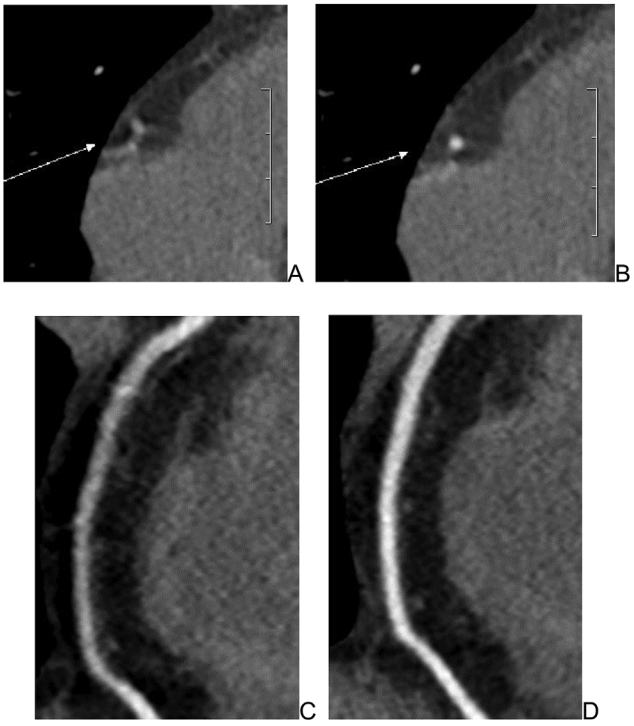

Fig. 1. Head-to-head comparison between primary and secondary reconstructions. Axial and curved plannar reconstruction (CPR) images of right coronary artery (RCA) at 45% R-R interval after primary reconstruction (A, C) and after secondary reconstruction with application of motion correction algorithm (B, D) in a patient with heart rate of 101 bpm.

After cardiac multi-phase reconstruction and automated coronary vessel tracking, the motion correction algorithm used information from adjacent cardiac phases within a single cardiac cycle to characterize vessel motion, including both path and velocity, determined actual vessel position at the prescribed target phase, and compensated for any residual motion at that phase. Fig. 1 shows an example of the impact of motion correction algorithm in a patient with heart rate of 101 bpm. Mean overall image quality was high and was similar between the two groups (group A, 1.49 ± 0.62; group B, 1.53 ± 0.67; P = .647). No significant differences were found between the two methods for patients with low heart rates (< 61 bpm) (group A1, 1.05 ± 0.23; group B1, 1.09 ± 0.29; P = .465), intermediate heart rates (61-75bpm) (group A2, 1.50 ± 0.54; group B2, 1.48 ± 0.58; P = .650), and high heart rates (> 75bpm) (group A3, 1.72 ± 0.75; group B3, 1.87 ± 0.78; P = .177). Results showed that for the two methods, image quality of patients with lower heart rates was better than those with higher heart rates. Table 2 and Fig. 2 show no significant differences of image quality score between the two groups and between subgroups with the same heart rate, and image quality of patients with lower heart rates was better than those with higher heart rates in terms of motion artifact. Two segments (from 2 different patients) in group A and 3 segments (from 3 different patients) in group B were classified as non-evaluable due to severe motion artifacts (all in group A3 or B3).

22 patients in group A (A_{ICA}) and 24 in group B (B_{ICA}) underwent ICA after CCTA within two weeks. Table 3 compares the diagnostic accuracy parameters of coronary CT angiography with those of ICA in the detection of stenosis of more than 50% in the two groups in a segment-based analysis. Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were 82.1%, 96.8%, 92.0%, 92.3% and 92.2%, respectively, in the breath-holding group and 82.2%, 96.6%, 91.4%, 92.5% and 92.2%, respectively, in the free-breathing group. Fig. 3 shows an example of correct detection of stenosis of more than 50% with free-breathing CCTA confirmed by ICA.

4. Discussions

Coronary computed tomography angiography (CCTA) is usually performed during breath holding after inspiration to avoid motion artifacts caused by respiration. However, some patients are not able to follow the breathing command and therefore cannot hold their breath sufficiently due to deafness, hearing weakness, severe pulmonary disease, or lack of cooperativeness. In these patients, conventional CCTA scan methods may result in major stair-step artifacts which often hamper a sufficient evaluation of the coronary arteries. Moreover, there are patients who cannot cooperate with repeated breathing exercises to hold their breath because of an emotionally nervous state. Some patients may present non-negligible heart rate variability during breath-holding. Therefore, it is with great clinical significance to have a scanning method enabling CCTA during free breathing.

So far, the possibility of free-breathing CCTA has been reported for 320-detector CT with the largest z-axis coverage of 16 cm and dual-source CT with high pitch. According to a report by Kang et al.,[7] the 320-detector CT allows for 16-cm z-axis coverage. Free-breathing CCTA using 320-detector CT did not show any significant difference in image quality from breath-holding CCTA for patients with heart rates lower than 75 bpm. Another report by Bischoff et al.[8] showed that in patients with low heart rate (< 60 bpm) who are not able to hold their breath adequately during CCTA images might also be acquired during free breathing without substantial loss of image quality when using a high pitch scan mode in dual-source CT. Main limitations of these two studies were the restriction to patients with low heart rates and lack of evaluation of diagnostic performance of free-breathing CCTA compared with conventional breath-holding scan protocols using ICA results as reference. According to our understanding, no studies have evaluated the feasibility of free-breathing CCTA without heart rate control and

Table 2
Subjective image quality score distribution of the sub-heart rate groups in Group A and Group B.

	Group A				Group B			
HR Range (bpm)	N	Avg. HR (bpm)	Score Distribution (1/2/3/4)	Avg. Score	N	Avg. HR (bpm)	Score Distribution (1/2/3/4)	Avg. Score
all	325	70.8 ± 13.8	185/123/15/2	1.49 ± 0.62	291	70.7 ± 13.2	163/106/19/3	1.53 ± 0.67
< 61	56	54.2 ± 4.0	53/3/0/0	1.05 ± 0.23	56	55.7 ± 11.3	51/5/0/0	1.09 ± 0.29
61-75	169	66.9 ± 4.6	88/78/3/0	1.50 ± 0.54	145	66.8 ± 4.5	81/58/6/0	1.48 ± 0.58
> 75	100	86.5 ± 12.3	44/42/12/2	1.72 ± 0.75	90	86.3 ± 10.9	31/43/13/3	1.87 ± 0.78

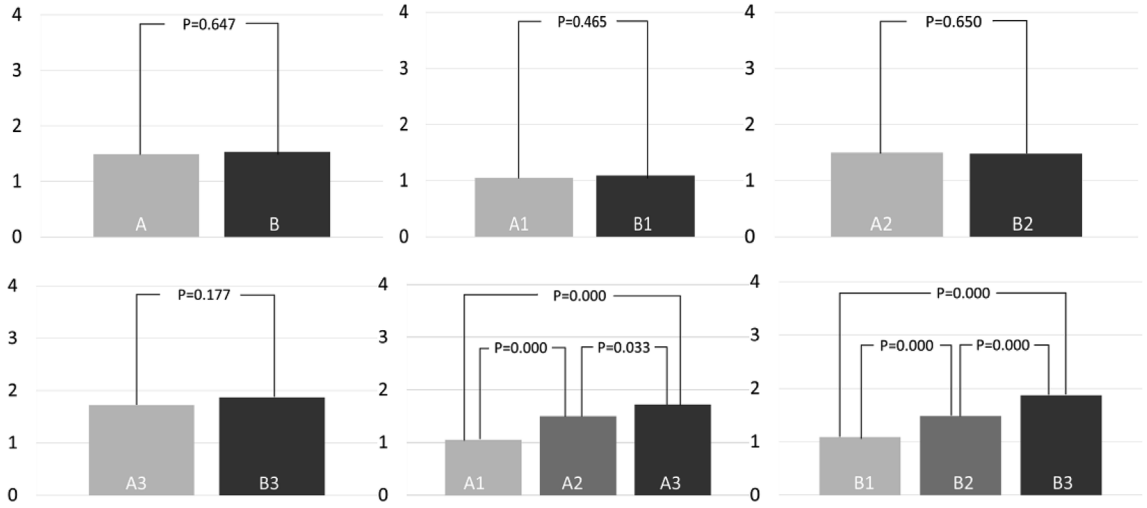

Fig. 2. Image quality scores of group A and B, and each subgroups. No significant differences were found between the two methods. Image quality of patients with lower heart rates was better than those with higher heart rates.

Table 3
Segment-based comparison of the diagnostic accuracy of coronary CT angiography in the detection of significant (> 50%) stenosis between the two groups.

	No. of Segments	No. of TN Findings	No. of TP Findings	No. of FN Findings	No. of FP Findings	Sensitivity	Specificity	PPV	NPV	Accuracy
A_{ICA}	270	180	69	15	6	82.1	96.8	92.0	92.3	92.2
B_{ICA}	295	198	74	16	7	82.2	96.6	91.4	92.5	92.2
P-value	–	–	–	–	–	0.989	0.917	0.885	0.934	0.993

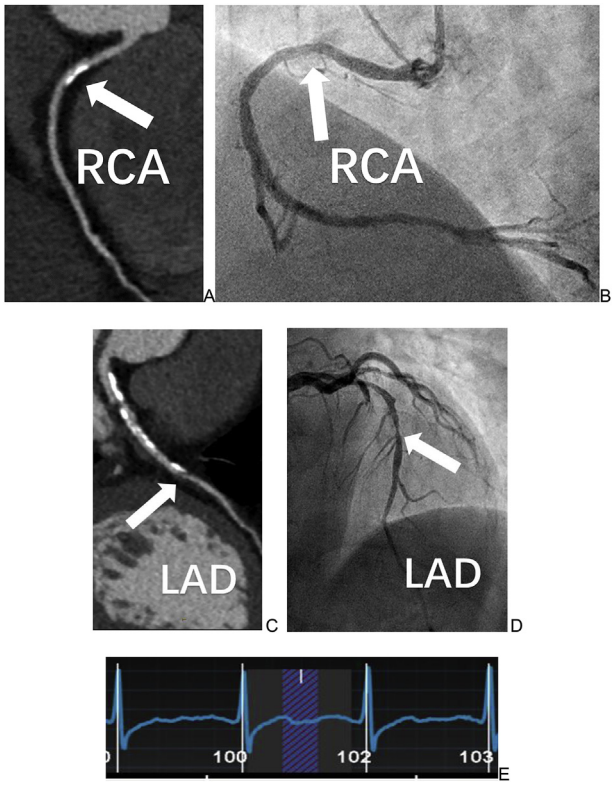

Fig. 3. Free-breathing coronary CT angiography was performed in a 62-year-old woman suspected of having CAD with heart rate of 102 bpm during acquisition. CCTA images enabled us to evaluate the coronary tree with good image quality and without motion blurring. Significant stenosis was identified in the proximal segment of RCA (A) and mid-segment of LAD(C) by CCTA. The stenosis was confirmed by ICA (B, D). Electrocardiogram showed acquisition was performed within one single cardiac cycle at a heart rate of 102 bpm(E).

compared the results with ICA.

Many studies have reported the advantages of 16-cm z-axis coverage including reducing the amount of contrast media, CCTA applications for patients with atrial fibrillation or high heart rates, and prospective ECG-gated CT angiography for the comprehensive evaluation of the whole aorta and coronary arteries.[12–15] The greatest advantage of the 16 cm z-axis coverage CT systems is the ability to achieve iso-phasic and iso-chronic CT data acquisition without stair-step artifacts. Due to this wide volume coverage, these CT machines are able to perform an axial, electrocardiogram (ECG)-gated examination of the heart during one R-R interval without movement of the table, and CCTA for the entire heart can be performed in a fraction of a second. This much improved temporal resolution in z-axis greatly reduces the impact of respiratory motion, which has a cycle time of several second, on coronary arteries. Another feature our study was based on was a secondary reconstruction incorporating the motion correction algorithm with the aim of compensating for coronary motion blurring. It was reported that secondary reconstruction using motion correction algorithm significantly improves coronary evaluability due to the significant reduction of severe motion artifacts with a marked improvement of image quality score when compared with the primary reconstruction that did not use the motion correction algorithm.[16–19]

Our study results indicated that based on the 16-cm z-axis coverage and motion correction algorithm, the free-breathing CCTA protocol in this study enabled us to evaluate coronary arteries with excellent image quality, and remarkable diagnostic accuracy despite high heart rate during the acquisition. Image quality, radiation dose, and diagnostic accuracy in patients with free-breathing were comparable with those with breath-holding. Indeed, sensitivity, specificity, negative predictive value, positive predictive value and accuracy of free-breathing CCTA were 82.2%, 96.6%, 92.5%, 91.4%, and 92.2%, respectively, in a segment-based analysis based on a 50% threshold against the standard of ICA findings. Although results showed that image quality of patients with lower heart rates was better than those with higher heart rates in terms of motion artifact, good image quality and diagnostic performance were observed in patients with higher heart rate in group B3

(> 75bpm).

There were some limitations to this study. First, we did not examine same patient with both free-breathing and breath-holding, and therefore we were unable to compare the two methods directly. Second, although our study population was the largest reported in the literature on free-breathing CCTA, the sample size of patients underwent both CCTA and ICA in our study was still relatively small, which may affect the statistical results for the diagnostic accuracy analysis. In addition, since only 18 subjects in both groups were examined with heart rate more than 100 bpm, whether the success of free-breathing CCTA can be extrapolated to higher heart rates needs further evaluation. Third, the results of our study were limited to 16-cm z-axis coverage CT scanners with motion correction algorithm. We were unable to perform the comparison in image quality and diagnostic accuracy with and without motion correction, for determining the additive effect of the motion correction to improve image quality and diagnostic accuracy.

In conclusion, free-breathing CCTA protocol used in our study did not show any significant difference in image quality, radiation dose and diagnostic performance from breath-holding. For patients with difficulties in holding their breath, free-breathing CCTA during a single cardiac cycle using scanners with 16-cm z-axis coverage and motion correction algorithm can be an alternative solution for coronary artery evaluation.

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